

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
21 July 2005 (21.07.2005)

PCT

(10) International Publication Number
WO 2005/066362 A3

(51) International Patent Classification:
C12N 9/10 (2006.01) C12Q 1/68 (2006.01)

(21) International Application Number:
PCT/EP2005/000064

(22) International Filing Date: 7 January 2005 (07.01.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
04000398.0 10 January 2004 (10.01.2004) EP

(71) Applicant (for all designated States except US): BAYER
HEALTHCARE LLC [US/US]; 555 White Plains Road,
Tarrytown, New York, 10591 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): STROPP, Udo
[DE/DE]; Suitbertusweg 8, 42781 Haan (DE).

(74) Agent: BURKERT, Frank; Bayer HealthCare AG, Law
and Patents, Patents and Licensing, 51368 Leverkusen
(DE).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
22 June 2006

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: HAPLOTYPES AND POLYMORPHISMS LINKED TO HUMAN THIOPURINE S-METHYLTRANSFERASE DE-
FICIENCIES

(57) Abstract: Haplotypes and polymorphisms of thiopurine S-methyltransferase (TPMT) are described that are linked to TPMT
deficiencies which can cause potentially fatal toxicity when patients are treated with thiopurines like mercaptopurine, azathioprine, or
thioguanine. The mutant alleles as well as PCR fragments, kits and methods for assaying the TPMT genotype of individual patients
are disclosed. Furthermore, algorithms are disclosed that combine the genotypes of a set of single nucleotide polymorphisms to
haplotypes that give a distinct information about the TPMT phenotype.

WO 2005/066362 A3